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Ambiguous emotion recognition in temporal lobe epilepsy: the role of expression intensity.

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Running title: Ambiguous emotions recognition in TLE.

Ambiguous emotion recognition in temporal lobe epilepsy: the role of expression intensity.

Abstract

The lateralization of emotion processing is currently debated and may be further explored by examining facial expression recognition (FER) impairments in Temporal Lobe Epilepsy (TLE). Furthermore, in individuals with TLE there is debate whether FER deficits are more pronounced in right than left. To shed light on this issue, individuals with TLE were tested with a FER task designed to be more sensitive than those classically used. Twenty-five right and thirty-two left TLE patients, candidates for surgery, and controls underwent a FER task composed of stimuli shown not only at full blown intensities (100%) but also morphed to display lower intensity levels (35%, 50%, 75%). Results show that, compared to controls, right TLE patients show deficits in the recognition of all emotional categories. Furthermore, when considering valence, right TLE patients are impaired only in negative emotions recognition, but no deficits for positive emotions have been highlighted in left TLE patients. Finally, only right TLE patients impairment was found to be related to the age of epilepsy onset. Our work demonstrates that FER deficits in TLE span across multiple emotional categories and manifest depending on the laterality of the epileptic focus. Taken together our findings provide strongest evidence for the Right Hemisphere Model, but also partial support for Valence Model. We suggest that actual models are not exhaustive to explain emotional processing cerebral control and that further multistep models should be developed.

Keywords: emotional dominance, facial expressions, FER, temporal lobe epilepsy, expression intensity, emotional lateralization**.**

1. INTRODUCTION

Although initial research indicated a dominant role of the right hemisphere in emotional processing more recent research has indicated that both hemispheres contribute to emotion processing (Demaree, Everhart, Youngstrom, & Harrison, 2005). Brain structures that are critically involved in emotional processing, such as the amygdala and the temporal cortices (Adolphs, 2010; Haxby, Hoffman, & Gobbini, 2000; Olson, Plotzker, & Ezzyat, 2007) are affected by Temporal Lobe Epilepsy (TLE) which is typically lateralised in focus making the condition a window for the understanding of the laterality of emotion processing.

According to the Right Hemisphere Model (RHM), the right hemisphere is responsible for perception, expression and experience of emotions (Borod, Koff, & Caron, 1983; Gainotti, 1983; Heilman & Bowers, 1990; Wager, Phan, Liberzon, & Taylor, 2003). This is supported by empirical evidence both from typical individuals and those with brain damage. For instance, emotional faces presented to the left visual field (and so initially processed by the right hemisphere) are better discriminated (Landis, Assal, & Perrett, 1979), rated as more intense (Levine & Levy, 1986) and elicit greater autonomic response (Spence, Shapiro, & Zaidel, 1996). Similarly, Benowitz et al., (1983) found that when a split brain patient was facial expression items specifically to each hemisphere separately they only showed difficulties in FER when the stimuli were presented to their left hemisphere. Studies of individuals with TLE typically report poor facial expression recognition only in right lateralized epilepsy (Benuzzi et al., 2004; Bonora et al., 2011; McClelland et al., 2006; Meletti et al., 2009; Meletti, Benuzzi, Nichelli, & Tassinari, 2003; Meletti, Benuzzi, Rubboli, et al., 2003).

The above research may however be an oversimplification, the Valence Model (VM) suggest that both hemispheres participate in emotional processing with different contributions depending on the emotional valence of the stimulus: positive emotions being processed by the left hemisphere while negative by the right (Davidson, 1992; Gur, Skolnick, & Gur, 1994; Silberman & Weingartner, 1986). Like the right hemisphere module, the VM is supported evidence both from typical individuals. For example, positive emotional faces are recognized faster within the right visual field, while negative faces within the left visual field (Reuter-Lorenz, Givis, & Moscovitch, 1983). However, evidence from individuals with brain damage is not so clear: impairments in the recognition of positive emotions in individuals with left hemisphere damaged is not always observed (Adolphs et al., 1996; Borod et al., 1998). In TLE, results from FER tasks are mixed, with some studies showing impaired recognition of several negative emotions (i.e., anger, fear, disgust and sadness) (Brierley, Medford, Shaw, & David, 2004; Meletti et al., 2009; Meletti, Benuzzi, Rubboli, et al., 2003), and others pointing towards a selective impairment of fear recognition only (Adolphs, Tranel, Damasio, & Damasio, 1994; McClelland et al., 2006; Meletti, Benuzzi, Rubboli, et al., 2003). A single study found FER impairments also in left TLE patients (Meletti et al., 2009) which authors explain in terms of inter-individual differences in the strength of emotional processing lateralization, with some individuals having less lateralized functions on the right. One explanation that the authors provide for their results is that impairments their participants with left lateralized TLE could be due to bilateral damage undetected by conventional MRI which had been found to show a unilateral hippocampal sclerosis when other methods such as PET show bilateral damage (Meletti et al., 2009). However, using this argument, if MRI is not sensitive enough to detect subtle bilateral damage, impairments for patients with right TLE could as well be caused by undetected left temporal damage. A further study found an impairment limited to fear recognition in left TLE (Reynders, Broks, Dickson, Lee, & Turpin, 2005). This last finding, in combination other studies that do not report clear cut differences based on the epileptogenic area lateralization (Benuzzi et al., 2004; Brierley et al., 2004), means that overall there is no clear cut support for either the right hemisphere or valence models emotional processing.

Based on divergent findings above, different versions of the VM have been developed (Gainotti, 2012). The approach-withdrawal model (Davidson, 1992), for instance, postulates that anterior prefrontal regions of the left hemisphere mediate approach behaviors, while anterior prefrontal regions of the right hemisphere mediate withdrawal behaviors. Despite similarities between the VM and the approach-withdrawal model, there are also noticeable differences: for instance, in the approach-withdrawal model anger would be grouped with happiness as an approach behavior but in VM would be groups with other negatively valenced emotions (Demaree et al., 2005).

Even taking into account new models, recent experimental findings still do not differentiate between the above models and evidence often conflicts (Gainotti, 2012). As an alternative, Gainotti suggests that the level of processing (conscious vs unconscious) might explain these diverse findings as most studies with finding opposing the right hemisphere model have adopted a cognitive (categorization) task, rather than using an unconscious perception task which Gainotti concludes are right hemisphere lateralized owing to a fast subcortical right hemisphere route for emotion processing (Gainotti, 2012). In TLE findings supporting the right hemisphere model have been obtained through categorization tasks that involve the left rather than the right hemisphere (Gainotti, 2012).

The use of low intensity facial expressions, obtained through the morphing technique, may help to distinguish the role of lateralization and to identify subtle impairments that might be associated with left TLE (Benuzzi et al., 2004; Brierley et al., 2004; Meletti et al., 2009). In other words the greater sensitivity required to recognize morphed stimuli, particularly those of low intensity, might help determine which model is supported by TLE data. The Ekman and Friesen pictures series (1976) is often by used to evaluate FER in TLE and is composed of full blown emotional expressions. However, previous studies on unimpaired subjects have shown the relevance of using not full blown expressions. When facial emotions are presented at lower intensities, individuals find them more difficult to recognize, limiting ceiling effects (Law Smith, Montagne, Perrett, Gill, & Gallagher, 2010). For example, Hoffmann, Kessler, Eppel, Rukavina and Traue (2010) failed to show gender differences in unimpaired subjects with full intensity stimuli, while gender differences emerged when varying the intensity of the expressions. This use of various facial expression intensities has been applied also to several pathologies, such as Autism Spectrum Disorders, resolving the dilemma on these subjects' ability to discriminate basic emotions facial expressions (Law Smith et al., 2010); in Parkinson Disease, to clarify differences in disgust perception in medicated and unmedicated subjects (Sprengelmeyer et al., 2003), and with similar aims in Alzheimer Disease (Spoletini et al., 2008), schizophrenia (Huang et al., 2011) and depression (Anderson et al., 2011).

The main goal of the current study was to explore the role of the lateralization of the epileptogenic area using facial expression stimuli of varied intensity. A facial varied intensity facial expression test was administered to 25 right and 32 left individuals with TLE who were candidates for surgery. The use of morphed facial expression stimuli of different intensity was expected to increase the sensitivity of the test in detecting subtle deficits that may arbitrate between different theories of emotional laterality. In summary, following the right hemisphere model predictions, only right TLE patients would be expected to show impairment across all facial expressions, as the right hemisphere model postulates that right hemisphere is responsible for perception, expression and experience of all emotions (Borod et al., 1983; Gainotti, 1983; Heilman & Bowers, 1990; Wager et al., 2003). Previous studies on TLE have not shown totally convincing evidence for the right hemisphere model as they fail to show deficits in the recognition of happiness (Meletti et al., 2009) possibly as a results of ceiling effects due expressions of happiness being recognized very accurately, for example Ekman and Friesen (1976) report average accuracy for happiness recognition of 99.2% in typical participants. Possible ceiling effects for happy facial expression recognition also effect testing of the VM which predicts that right TLE patients should show impaired recognition of negative emotions, while left TLE in recognizing positive emotions. Similarly, the reduction in intensity of happy facial expressions through the use of morphing may make such an effect visible in the current experiment. Finally the approach-withdrawal model predicts a specific deficit in disgust, fear, and sadness (avoidance emotions) in right TLE patients, and in anger and happiness (approach emotions) in left TLE patients, considering that emotion recognition is accomplished by both temporal and prefrontal regions and that this network might be interrupted by TLE.

2. MATERIALS & METHODS

2.1 Participants

Sixty-six patients diagnosed with drug resistant temporal lobe epilepsy (TLE) (ILAE, 1993) were selected for the study. Patients were recruited from the “Claudio Munari” Centre for Epilepsy Surgery, Niguarda Ca’ Granda Hospital, Milan, and from the Epilepsy Centre, Neurology II, San Paolo Hospital, University of Milan, Milan. Patients were candidate for surgical treatment of epilepsy on the basis of clinical evaluation, EEG video monitoring and neuroimaging results. All patients had normal or corrected to normal vision and gave informed consent for participating in the study. The experiment has been conducted in accordance with the Declaration of Helsinki.

Before being recruited for the experiment, patients underwent a neuropsychological evaluation, involving the assessment of language (Token Test, Letter and Category Fluency Test, Boston Naming Test), episodic memory (Short Story Recall), verbal and non-verbal short term memory (Digit Span Forward Task, Corsi Block Tapping Task) and memory for faces (Camden Recognition Test), executive functions (Trail Making Test, Attentive Matrices), visuo-spatial processing (Benton Line Orientation Test), abstract reasoning (Raven's Coloured Progressive Matrices) and depression (Beck depression Inventory-BDI). Anxiety was assessed through a psychiatric clinical colloquium. Patients performing in the normal range at all these tasks were recruited for the experiment, to avoid mixed results due to cognitive impairments rather than emotional deficits. Inclusion criteria to participate in the study were: (i) age between 16 and 70 years; (ii) absence of mental deterioration, as confirmed by the neuropsychological testing; (iii) preserved perceptual functioning and memory for faces as evidenced by normal performance on the Benton Line Orientation Test and the Camden Recognition Test; (iv) preserved executive functions and abstract reasoning as confirmed by Trail Making Test, Attentive Matrices, Raven's Coloured Progressive Matrices; (v) absence of dementia (DSM-IV TR diagnostic criteria for dementia (American Psychiatric Association, 2007)), sensory or motor deficits and psychiatric illness; (vi) absence of mood disorder or suspected depression, as highlighted by the BDI and by the psychiatric assessment. Antiepileptic drugs (AEDs) were not considered as an exclusion criteria since our patients showed no cognitive side effects due to drug treatment. Patients were tested on average one month prior to surgery. Neuropsychological and FER tests were administered in separate sessions and not during neuroimaging or EEG examinations. Of the sixty-six patient recruited, 10 were excluded due to pathological scores at the neuropsychological tests. Thus, the final sample was composed by 56 individuals (Table 1).

Thirty-two patients had the *focus epilepticus* in the left hemisphere and twenty-four in the right hemisphere (Table1). Left and right side patients did not differ with respect to age ($t_{(54)}$=.945, p=.349), sex (χ^2= 0.024, p=.876), educational levels (χ^2=3.905, p=.272) and Raven's Coloured Progressive Matrices scores ($t_{(54)}$=0.757, p=.453). Furthermore, we did not find any significant difference in the distribution of epilepsy onset between left and right TLE patients (χ^2=1.904, p=.593). Fifty-four age and sex matched control subjects were also recruited from the subject pool of the University of Pavia. Controls were referred on the basis of an absence of previous history of mental illness and completed the Raven's Coloured Progressive Matrices test to confirm preserved perceptual and executive functioning. Compared to the control group, both right and left TLE patients showed no significant differences in distribution of gender and age (all p>.05). However, patients groups showed both fewer years of education (Kruskall-Wallis χ^2=42.447, p<.001) and lower scores on the Raven's Coloured Progressive Matrices when compared to controls (Kruskall-Wallis χ^2=13.646, p=.001). Even though patients performed worse than controls on the Raven's Coloured Progressive Matrices, their performance was still within the normal range according to the Italian normative values (Caffarra, Vezzadini, Zonato, Copelli, & Venneri, 2003).

			Patients		**Controls (n=54)**
			Right TLE (n=24)	**Left TLE (n=32)**	
De mo	**Age**		35.33 (± 11.06)	38.31 (± 12.11)	35.7 (± 11.35)
	Education	0-5 years	5	2	-

graphic Features		6-8 years	3	9	1
		9-13 years	12	16	12
		> 13 years	4	5	41
	Gender	Males	14	18	23
		Females	10	14	31
	Hand Dominance	Left	1	3	4
		Right	23	29	50
Clinical Features	**Raven's Coloured Progressive Matrices**		29.59 (5.64)	30.86 (5.86)	33.55 (2.46)
	Type	MTS	18	24	-
		Other	7	8	-
	Onset	0-1 years	1	2	-
		2-6 years	4	3	-
		7-12 years	7	6	-
		>13 years	12	21	-
	Frequency	less than 5 seizures per month	18	23	-
		between 25 & 5 seizures per month	4	8	-
		between 26 & 50 seizures per month	2	1	-

Table 1. Demographic and clinical features of the right and left TLE patients and the control group. Age and Raven's Coloured Progressive Matrices test score are presented as Mean (Standard Deviation), while the other variables are presented as number of subjects for each category. MTS = mesial temporal sclerosis.

2.2 Apparatus & Procedure

The Animated Full Facial Expression Test - Revised (AFFECT-R) is a computerized test created to investigate FER. The test was modeled on the FER task used in Gagliardi et al. (2003). In the AFFECT-R, five basic facial emotion expressions (fear, disgust, anger, sadness, happiness), expressed by four individuals (two males and two females) from the Ekman and Friesen (1976) series are displayed. In the current experiment, the five basic expressions of anger, disgust, fear, happiness and sadness were displayed at four intensity levels: 35%, 50%, 75% and 100% (Figure 1). The intermediate levels (35%, 50% and 75%) were obtained using a morphing technique (Benson & Perrett, 1991; Tiddeman, Burt, & Perrett, 2001), that allows to change (morph) the neutral into the full intensity (100%) expression (software: Psychomorph, Tiddeman, Burt, & Perrett, 2001). Surprise was not used as previous studies had reported that even unimpaired subjects frequently mistake this emotion for fear (Rapcsak et al., 2000).

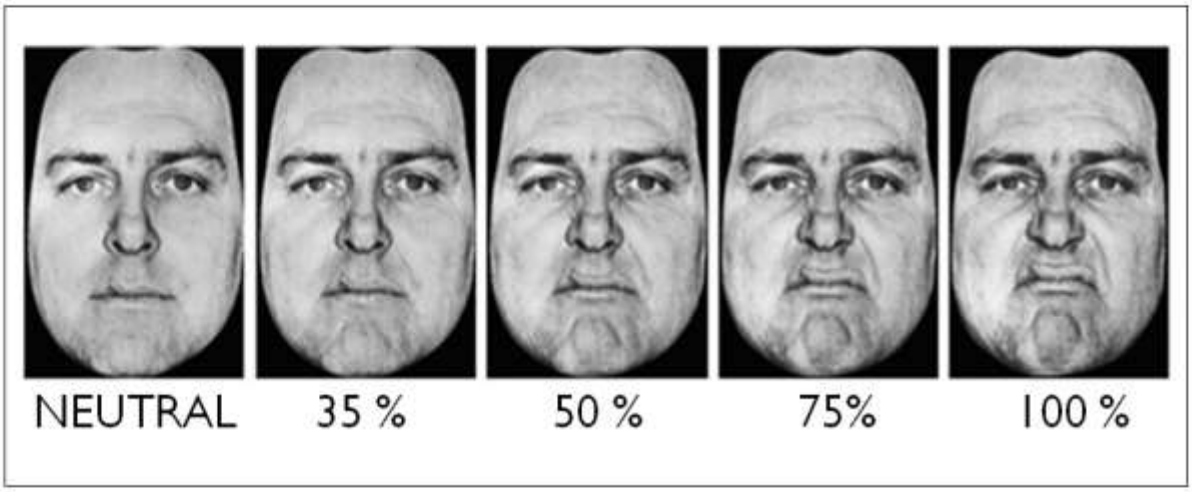

Figure 1. Example of the AFFECT-R stimuli. From left to right, the different expression intensities for disgust are depicted by the male individual. The first image display the neutral face (0% intensity), while the last depict the full blown intensity (100%). In-between images (35%, 50% and 75%) display intermediate intensities obtained using the morphing technique.

We presented the AFFECT-R on a 15” (30 cm x 23 cm) touch screen (VIDI LCD VL150 C/T, model “comfort xp”, CA&G ELETTRONICA srl) with a screen resolution of 1024 x 768 pixels. Pictures had the size of 14.7 cm high and 7.6 cm wide, covering a vertical visual angle of 16.72°. On each trial, one image was shown in the centre of the screen, and five labels (corresponding to the emotions presented on the test) were shown below (Figure 2). With their dominant hand participants had the task to touch the on-screen label that best represented the emotion depicted. Participants were asked to answer as fast and as accurately as possible, but there was no time limit to complete a trial. The order of the emotion labels was randomized between subjects. Participants did not receive any feedback on their performance during the experiment. Accuracy was collected for each trial.

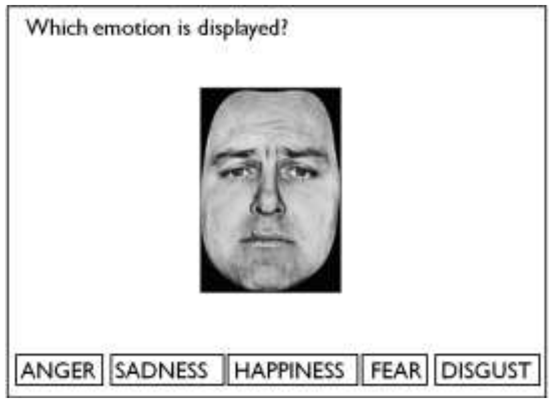

Figure 2. Example of an AFFECT-R trial. The emotional expression is shown in the centre of the screen and the five answer labels (each one corresponding to one of the five emotions presented on the test) are shown below it. Participants had to press the label that best corresponded to the facial expression. Labels were randomised across the experiment.

At the beginning of the experiment, participants were presented with 5 practice trials (one for each emotion) in a random order. During this practice, emotions were expressed at full intensity to familiarize participants with the task. After the practice trials, participants started with the four experimental blocks of the AFFECT–R, where they were shown a total of 80 stimuli (16 for each emotion, 4 for every intensity level). Blocks were randomized between subjects and included twenty stimuli each. The experiment took about twenty minutes to be completed.

2.3 Statistics

Data were analysed using Statistical Package for Social Sciences (SPSS 13.0, Chicago, IL, U.S.A.). The percentage of correct answers (Accuracy) (see Table 2 in the Supplementary materials for average raw scores) was transformed into z-scores to normalize the data. FER scores were analysed using a repeated measures ANOVA, with Emotional Category (anger, fear, disgust, sadness and happiness) and Stimulus Intensity (35%, 50%, 75% and 100%) as within subject factors, and Group (controls, left and right TLE patients) as a between subject factor. Alpha level was set at .05. Further ANOVAs and post-hoc comparisons (Bonferroni corrected) were then performed according to the main effects and interactions resulted from the previous analysis,

Finally, to test the "early-onset" hypothesis (that right amygdala damage before 6 years results in permanent FER impairments in TLE patients, while a later epilepsy onset leaves intact FER abilities (Hlobil, et al. 2008; Meletti, et al. 2003b)) we performed Spearman's rank correlations between age at epilepsy onset (categorical variable) and FER accuracy.

3. RESULTS

3.1 Between Group Analysis

The repeated measures ANOVA performed on the percentage of correct answers (see Table 2 in the Supplementary materials for average raw scores) revealed a significant three way interaction between Emotional Category, Stimulus Intensity and Group ($F_{(24,\ 1284)} = 2.120$; $p = .001$). No other significant main effects or interactions were found. As patients and controls had different levels of education, we re-ran this main analysis including education as covariate. This control did not change the results, the three way interaction still the only significant finding. Thus, we conclude that differences in FER are not due to differences in education.

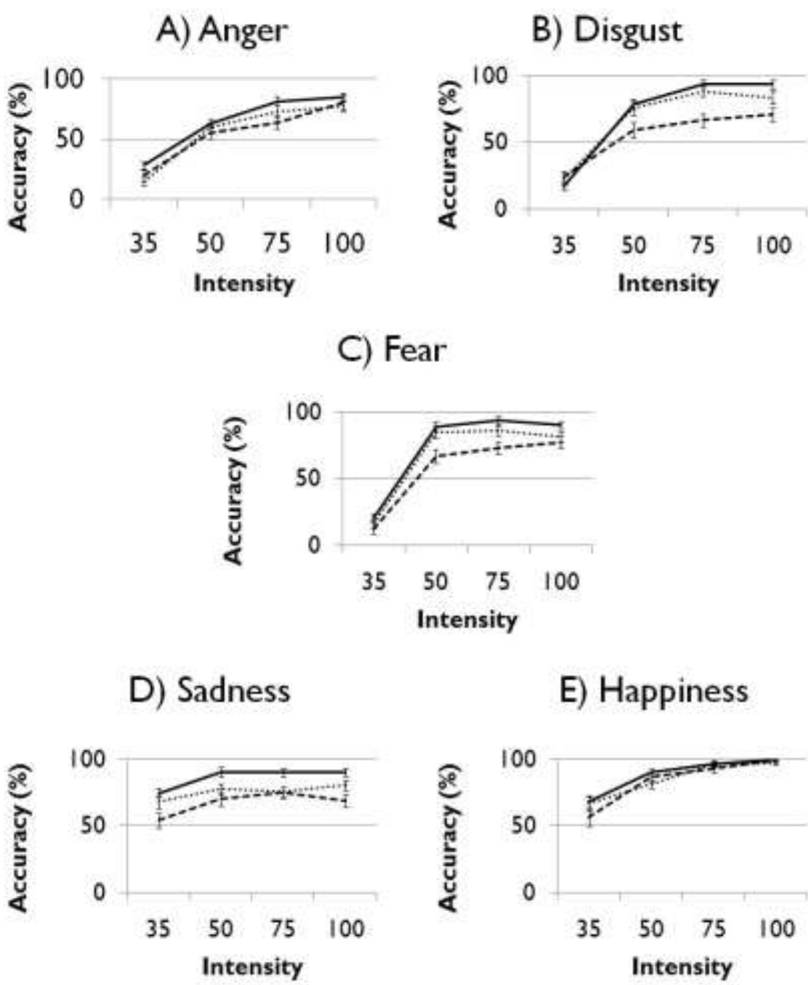

Figure 3. Percentage of correct answers (accuracy) for each emotion depicted as a function of display intensity. Bars represent standard error of the mean. Black lines = controls. Dashed lines = right TLE patients. Dotted lines = left TLE patients.

To further explore the Emotional Category * Stimulus Intensity * Group interaction, we performed separate ANOVA for each intensity level with the factor Emotional Category and Group.

At 35% of intensity, there was a significant main effect of Group ($F_{(2, 107)}$ = 4,480; p = .014), but no other effects or interactions. Post hoc tests of the main effect of Group revealed that right TLE patients perform significantly worse than controls (mean difference -.322; p=.014). Interestingly, no differences between right and left TLE emerged, or between left TLE and controls (all ps > .05).

At 50% of intensity, a main effect of Group ($F_{(2, 107)}$ = 4.480; p = .014) and a strong trend towards significance for the Emotional Category * Group interaction ($F_{(8, 428)}$ = 4.480; p = .059) emerged. Post hoc analysis (estimated marginal means comparisons) of the main effect of Group revealed a significantly worst performance of right TLE patients than controls (mean difference -.550 p=.003) but no differences between left and right TLE and left TLE and controls (all ps > .05). To explore the interaction between Emotional Category and Group, we performed a further ANOVA for each emotion. These analyses revealed a significant difference between groups for disgust ($F_{(2,107)}$ = 4,179; p = .018), fear ($F_{(2,107)}$ = 6,136; p = .003) and sadness ($F_{(2,107)}$ = 6,230; p = .003) recognition. Post hoc comparisons showed that for disgust recognition the effect was due to significantly worst performance of right TLE patients when compared to controls (mean difference: - .678; p = .016). Similarly, right TLE patients were poorer than controls in recognizing sadness (mean difference: - .773; p = .004). However, for fear recognition not only did right TLE patients perform significantly worse than controls (mean difference: -0.815; p = .002), but they also performed significantly worse than left TLE patients (mean difference: -.649; p = .040).

At 75% of intensity, a main effect of Group ($F_{(2,107)}$ = 11,008; p < .001) but no other effects or interactions was found. Post hoc analysis revealed significantly worst performance of right TLE patients than controls (mean difference -.700; p <.001). Interestingly, we also found a significant difference between right and left TLE (mean difference -.408; $p = .046$), with right TLE patients performing worse than left TLE. No differences between left TLE and controls emerged ($p > .05$).

At 100% of intensity, there was no significant effect of Group, Emotional Category, or interaction between factors (all ps > .05).

In summary, our data show clearly show a general compromising in right TLE patients, that is not specific to emotional category at 35% and 75% intensity. In comparison, at 50% intensity effects differ between emotional categories. In particular, fear recognition is more compromised in right TLE compared to both controls and left TLE. Generally, even with morphed stimuli, the left TLE did not show impairments in FER recognition. Finally, no significant differences were found for the 100% displays of stimuli.

3.2 Valence Analysis

According to the VM, right TLE patients should show an impairment in recognizing negative emotions, while left TLE in recognizing positive emotions. The consideration of negative emotions separately in the previous analysis could have masked effects of valence. In an attempt to unmask these effects, we explored the data further by grouping emotional categories into positive (happiness) and negative (averaged answers for anger, fear, disgust and sadness) emotions (Valence). Then, we applied a repeated measures ANOVA, with Group, Stimulus Intensity and Valence as factors. There was a significant main effect of Group ($F_{(2, 107)} = 5{,}985$; $p = .003$), which post-hoc tests showed was due to worse performance of right TLE compared to controls (mean difference: - .417). Furthermore, the analysis revealed a significant three way interaction between Group, Stimulus Intensity and Valence ($F_{(6, 321)}$ = 2,246; p = .047). Follow up ANOVAs at each intensity level showed a significant interaction between Valence and Group only at 50% of intensity ($F_{(2, 107)}$ = 3,365; p = .038). Further exploration of this interaction revealed that the effect is driven by a significant difference between groups for Negative Emotions ($F_{(2, 107)}$= 6,689; p=.002), explained by a worst performance of right TLE patients with respect to controls (mean difference: - . 636; p = .002).

In summary, the effect of valence emerged only for 50% intensity displays and indicated a compromising in negative emotions only in right TLE patients.

3.3 Correlation with age at epilepsy onset

Finally, we investigated correlations between FER and age at epilepsy onset, as this last variable has been frequently assumed as supporting the RHM in epilepsy (Hlobil, Rathore, Alexander, Sarma, & Radhakrishnan, 2008; Meletti et al., 2009; Meletti, Benuzzi, Rubboli, et al., 2003). We considered the overall performance at the FER task, independently from the emotional category and the stimulus intensity. There was not significant correlation for left TLE patients ($p > .05$), while right TLE patients showed a significant positive correlation between age at epilepsy onset and FER accuracy (ρ = .562; p = .004). This last finding might indicate that if age at onset is later in life, FER performance is better. It should be remarked that we did not find significant differences in the onset distribution between left and right TLE patients. Thus, our results are unlikely due to an influence of the different number of subjects presenting a later disease onset among left TLE patients.

Taken together, our results confirm that age at onset influences right but not left TLE patients' performance, in agreement with previous findings (Hlobil et al., 2008; Meletti, Benuzzi, Rubboli, et al., 2003).

4. DISCUSSION

Facial Expression Recognition (FER) has often been investigated Temporal Lobe Epilepsy (TLE) (Boucsein, Weniger, Mursch, Steinhoff, & Irle, 2001; Fowler et al., 2006; Golouboff et al., 2008; Hlobil et al., 2008; Meletti et al., 2009; Meletti, Benuzzi, Rubboli, et al., 2003) but there has been no agreement on whether FER impairments are greater in right TLE (Benuzzi et al., 2004; Bonora et al., 2011; McClelland et al., 2006; Meletti et al., 2009; Meletti, Benuzzi, Nichelli, et al., 2003; Meletti, Benuzzi, Rubboli, et al., 2003) or if also left TLE is characterized by FER deficits (Meletti et al., 2009; Reynders et al., 2005). Here, rather than use just full intensity faces (Ekman & Friesen, 1976) facial expression with different intensities were displayed to clarify the role of epilepsy lateralization in FER. The anatomical lateralization in TLE is normally clear making TLE a suitable model for exploring hemispheric dominance in emotional processing which may clarify if emotional processing is predominantly associated with the right hemisphere (Right Hemisphere Model – RHM) (Borod et al., 1983; Heilman & Bowers, 1990; Wager et al., 2003) or if there is a bi-hemispheric contribution to emotion recognition depending on the stimuli value (Valence Model – VM) (Davidson, 1992; Gur et al., 1994; Silberman & Weingartner, 1986). Compared to cerebrovascular damage and transcranial magnetic resonance (TMS), epilepsy presents several advantages. For instance, cerebrovascular damage is usually associated with a number of diverse cognitive impairments, particularly in the acute phase (Ferro, 2001). Furthermore, it is quite rare to observe a stroke patient presenting emotional deficits limited to “recognition”, while it is usually reported that patients are affected by productive symptoms concerning emotions (such as the catastrophic reaction or the depressive reaction) (Chemerinski & Robinson, 2000). Finally, aphasia is quite common after left stroke, and could hinder the use of a labeling task to explore FER (de Freitas, 2012). On the other hand, it is quite difficult to reach subcortical structures with techniques such as the TMS, because impairments caused by single pulses TMS are usually restricted to cortical areas (Walsh & Cowey, 2000), Furthermore an exact stimulation of the desired area cannot be guaranteed unless fMRI-guided TMS is used (Beauchamp, Nath, & Pasalar, 2010). In summary, there are several good reasons to consider TLE, a neurological disease affecting “emotional” areas, as a good and convenient model to study emotional processing disturbances and hemispheric dominance.

Through the use of more sensitive graded stimuli, we found that only right TLE patients show FER impairments that were independent of emotional category. Age at epilepsy onset was also found to impact FER in right TLE patients only supporting the “early-onset” hypothesis which suggests that right amygdala damage before 6 years of age results in permanent FER impairments (Hlobil et al., 2008; McClelland et al., 2006; Meletti et al., 2009; Meletti, Benuzzi, Nichelli, et al., 2003), preventing the functional cerebral reorganization and the development of an appropriate FER system (McClelland et al., 2006; Meletti et al., 2009). Even using various intensity stimuli, we found that age at epilepsy onset seems to be associated with right TLE patients’ performance only. These results are in agreement with the hypothesis that right temporal structures diffusely modulate different emotions (Adolphs, 2010; Fusar-Poli, Placentino, Carletti, Landi, et al., 2009). Considering the RHM predictions, we confirmed that only right TLE patients show impairment. Furthermore, this impairment concerns all emotional categories, congruently with the postulate that right hemisphere is responsible for all emotions (Borod et al., 1983; Gainotti, 1983; Heilman & Bowers, 1990; Wager et al., 2003)

However, at 50% of intensity we found a greater compromising of fear recognition in right TLE both respect to controls and left TLE, in agreement with previous studies that highlighted an impairment of fear recognition (Adolphs et al., 1994; McClelland et al., 2006; Meletti, Benuzzi, Rubboli, et al., 2003). Furthermore, at this intensity the observed deficit concerned only fear, sadness and disgust. Considering also the analysis of valence, our results are partly in agreement with studies showing impaired recognition of negative emotions (i.e., anger, fear, disgust and sadness) in TLE (Brierley et al., 2004; Meletti et al., 2009; Meletti, Benuzzi, Rubboli, et al., 2003) and more in general with with the idea that right temporal structures have a special role for negative stimuli (Davidson, 1992; Gur et al., 1994; Silberman & Weingartner, 1986). These results partly confirm the VM, according to which right TLE patients should show an impairment in recognizing negative emotions. However, even using more sensitive stimuli we have not been able to detect positive emotions impairments in left TLE.

Furthermore, results at 50% of intensity offer also partial support for the approach-withdrawal model that a specific deficit in disgust, fear, and sadness (avoidance emotions) in right TLE patients. However, also in this case, we failed to demonstrated the second part of the prediction, impairments in anger and happiness (approach emotions) recognition in left TLE patients.

It should be noticed that we employed only one positive emotion, to obtain comparable results to previous studies using the Ekman and Friesen series, but the use of one positive emotion might question the generalizability of the results for positive emotions. Recent studies investigating happiness recognition highlight an advantage for happy faces compared to other facial expressions (Calvo & Lundqvist, 2008; Calvo, Nummenma, & Avero, 2010). Furthermore, it seems possible that, at a basic level, there is only one positive emotion, happiness, making happiness recognition a simpler task than recognizing specific negative emotions (Adolphs et al., 1996). It should be considered that virtually all happy faces contain some variant of the stereotypic signal of this emotion, the smile (Adolphs et al., 1996). Nevertheless, other studies in TLE using only happiness as positive emotion have been able to highlight effects (Hlobil et al., 2008) and our results, at least for low intensities, are not at ceiling. Thus it seems unlikely that our findings are due to the use of happiness only.

Finally, the absence of significant differences for 100% of intensity is coherent with previous results showing lack of differences based on the epileptogenic area lateralization (Benuzzi et al., 2004; Brierley et al., 2004). This result in particular might indicate that in some cases full displays of emotions are not enough sensitive to assess impairments, further corroborating the hypothesis that more difficult stimuli are needed.

A recent meta-analysis considered emotional face processing in unimpaired subjects, performed on 105 studies that mainly used the Ekman and Friesen series (Fusar-Poli, Placentino, Carletti, Allen, et al., 2009). This work highlights that brain networks for facial emotional processing might be far more complex than what indicated by the RHM, the VM and the approach-withdrawal model, as the recognition of emotional faces seems to involve bilateral, widespread areas that include not only the limbic system but also the prefrontal and visual cortex (Fusar-Poli, Placentino, Carletti, Allen, et al., 2009). Moreover, these findings support the idea that the bilateral activation of some structures, such as the amygdala, might indicate a multistep processing during the decoding of emotional expressions (Adolphs, 2002a; Fusar-Poli, Placentino, Carletti, Allen, et al., 2009; Glascher, Tuscher, Weiller, & Buchel, 2004; Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004). According to this hypothesis, the right amygdala might be activated automatically by arousing stimuli, in a relatively global emotional reaction, while the left amygdala could be involved in a more detailed and cognitive information processing step, aimed at decoding emotional valence and magnitude (Adolphs, 2002b; Glascher et al., 2004). Our results are partly in agreement with this hypothesis, as we found a more general impairment and restricted to right patients only. However, given the difficulty of the stimuli, for instance at 35% of intensity, we cannot confirm that the role of the left amygdala in a more detailed and cognitive information processing step. Rather, considering a multistep model, it might be that the impairment in right structures is enough to preclude even later steps in the processing, preventing a compensation from the left structures and the activation of subsequent stations of the emotional network. Interestingly, the same voxel-based meta-analysis also shows that disgust recognition is processed in right subcortical and cortical structures (Fusar-Poli, Placentino, Carletti, Landi, et al., 2009). This finding is in line with the compromising of this negative emotion we found in right TLE patients. Particularly, it has been pointed out by several studies that disgust is processed by the insula (Phillips et al., 1998; Phillips et al., 1997; Sprengelmeyer et al., 1996), and depth electrodes studies performed in epilepsy patients further suggest that the crucial area of this structure is the ventral anterior part (Krolak-Salmon et al., 2003). Disgust is postulated to be different from other emotions, such as fear. A possible explanation for these differences, such as the later temporal responses found in ERPs studies (Krolak-Salmon et al., 2003), is that disgust has a different evolutionary meaning, being characterized by a broader conceptual knowledge related to moral disgust (a more cognitive component) and not only by a primitive and arousing environmental reaction (Krolak-Salmon et al., 2003; Rozin & Fallon, 1987). Moreover, the insula has extensive anatomical connections with temporal areas, such as the amygdala and the hippocampus, and several studies have pointed out its implication in TLE epileptic pathology (Schwartz, 2005). Even though there are still no available data to precisely compare the role of the right and the left insula (Krolak-

Salmon et al., 2003), it seems from our results that the right insula might be more involved in disgust processing than the left. However, our data should be cautiously considered, as we cannot establish to which degree the insula was involved in the patient group used for the study, and further studies on TLE could directly address this hypothesis.

A different explanation proposed for the contribution of the two hemispheres to emotional processing is that conscious and unconscious aspects of emotional processing could be mediated differently by the two hemispheres, with the right hemisphere more involved in unconscious and the left hemisphere more involved in conscious emotional processing (Gainotti, 2012). However, our results, similarly to previous studies (Meletti, Benuzzi, Rubboli, et al., 2003), seems to suggest that the right hemisphere plays an important role also in explicit emotional processing. Furthermore, as we adopted a task in which subjects were required to choose the correct label for an emotion without time constraints, our results are not in agreement with the idea that the left hemisphere is concerned with categorization or cognitive tasks using emotional material, whereas rapid detection tasks would imply the right hemisphere (Gainotti, 2012). However, as we did not adopted both kind of tasks, we cannot completely rule out the possibility of a difference between left and right hemisphere contribution according to the task. Further studies could directly compare tasks (categorization/detection) and type of processing (conscious/unconscious) in TLE, to further clarify this alternative hypothesis on hemispheric specialization. Finally, as we modeled our FER task on the basis of previously used protocols (Meletti et al., 2009; Meletti, Benuzzi, Rubboli, et al., 2003), we adopted a forced choice procedure in which participants did not have the possibility to choose a “neutral” answer. This might be an important task issue, as in other domains it has been demonstrated that differences in patients’ performance can arise from using different response criteria during clinical and forced-choice tests (Azzopardi & Cowey, 1998). Future studies could explore whether using a different procedure, allowing participants to answer that they do not see any emotion, might end up in diverse results.

Even though evidence from our data seems to provide a stronger support for the RHM, the partial support for the VM and the approach-withdrawal model that we also found suggests, to understand emotional lateralization and to formulate exhaustive models, to consider more widespread brain networks (Vuilleumier et al., 2004), to evaluate both conscious and unconscious processing (Gainotti, 2012) and to adopt stimuli of diverse arousal, valence and difficulty (Demaree et al., 2005). In our study, which was not aimed at directly compare dimensions of emotions, we nevertheless have been able to notice that results are mixed. Furthermore, the most interesting findings derived from stimuli at 50% of intensity. Thus, a comprehensive model should also be able to explain the relationship between these different components of emotional processing rather than considering them isolated, and to reach this goal the study of emotional processing in TLE, usually performed also to shed light on the issue of emotional lateralization, should make use of more sensitive experimental paradigms (Vuilleumier et al., 2004), that takes into account new models on the hemispheric contribution to emotional processing. While previous studies adopted mainly full intensity displays, in this experiment we used different intensity stimuli, that have been demonstrated to be more effective (Hoffmann et al., 2010; Law Smith et al., 2010). Future studies on FER in TLE could benefit from adopting more varied expressions. Particularly, our speculation is that TLE, instead of confirming the RHM or the VM, points towards the possibility of alternative and more comprehensive models of emotional lateralization that take into account also the multistep nature of this function.

Disclosure of Conflicts of Interest
None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Supplementary materials

		Control (n=54)	**Right TLE (n=25)**	**Left TLE (n=32)**
Emotion	Intensity	Mean (sd)	Mean (sd)	Mean (sd)
ANGER	35	28.24 (26.62)	19.79 (20.82)	**14.84 (15.37)***
	50	62.5 (25.58)	55.20 (27.56)	59.37 (26.75)
	75	81.01 (26.12)	**63.54 (31.26)***	72.65 (24.89)
	100	84.72 (26.34)	80.20 (26.56)	77.34 (27.21)
DISGUST	35	17.12 (21.62)	23.95 (28.05)	22.65 (23.21)
	50	78.7 (22.47)	**59.37 (39.57)***	75.78 (28.74)
	75	93.51 (14.72)	**66.66 (37.57)***	88.28 (20.06)
	100	93.51 (15.5)	70.83 (39.47)	83.59 (25.09)
FEAR	35	20.83 (20.46)	12.5 (14.74)	16.4 (20.68)
	50	88.88 (18.6)	**66.66 (37.35)***	84.37 (26.75)
	75	93.51 (11.6)	**72.91 (36.05)***	85.93 (21.94)
	100	89.81 (16.48)	**77.08 (31.2)***	81.25 (20.08)
HAPPINESS	35	68.05 (31.63)	56.25 (33.98)	66.4 (25.09)
	50	90.27 (17.79)	86.45 (18.03)	81.25 (19.05)
	75	96.29 (10.2)	92.7 (21.47)	96.09 (11.2)
	100	99.53 (3.4)	98.95 (5.1)	96.87 (8.4)
SADNESS	35	74.53 (24.52)	**54.16 (30.99)***	67.96 (28.56)
	50	90.27 (20.27)	**69.79 (34.56)***	77.34 (24.89)
	75	89.81 (17.18)	**75 (27.58)***	**75.78 (24.99)***
	100	89.81 (15.75)	**68.75 (32.34)***	80.46 (22.66)

Table 2. FER average accuracy (percentage of correct answers, raw data are presented). Means and standard deviations of the three groups are depicted for each emotion at each intensity. Emotions at which patients resulted worse than controls are indicated in bold and with an asterisk.